Review J Oncol Pharm Pract. 2026 Aug 5:10781552261470027.
doi: 10.1177/10781552261470027. Online ahead of print.

Depatuxizumab mafodotin in glioblastoma: A systematic review of efficacy, safety, pharmacokinetics and biomarker stratification

Hasan Matar [1], Bassel Alrabadi [1], Aseel Abu Ata [2], Zainab Bahdar [3], Maria Zagiczek [4]

PMID: 42554799 DOI: 10.1177/10781552261470027

Abstract

BackgroundGlioblastoma (GBM) is an aggressive primary brain tumor with a dismal prognosis. Alterations in the Epidermal Growth Factor Receptor (EGFR) in about half of the cases, represent a key therapeutic target. Depatuxizumab mafodotin (Depatux-M) is an antibody-drug conjugate (ADC) developed to deliver a cytotoxic payload specifically to EGFR-amplified tumor cells.AimThis systematic review aims to synthesize all available clinical evidence to evaluate the antitumor efficacy, safety profile, pharmacokinetics, and biomarker-based stratification for Depatux-M in the treatment of glioblastoma.MethodsA systematic literature search was conducted across PubMed, Scopus, Cochrane Library and Web of Science. After screening, 11 clinical studies involving a total of 1420 patients were included for analysis. Data on efficacy, safety, biomarkers, and pharmacokinetics were extracted and synthesized.ResultsThe review found that Depatux-M demonstrated modest antitumor activity, with objective responses and improved progression-free survival primarily observed in the molecular subgroup of patients with tumors harboring EGFR amplification and/or the EGFRvIII mutation. Pharmacokinetic data showed linear, predictable exposure with low potential for drug-drug interactions, notably with temozolomide (TMZ). Ocular toxicities were the most common adverse events, occurring in over 90% of patients; these were often reversible and manageable. The overall safety profile was considered acceptable.ConclusionDepatuxizumab mafodotin presents a targeted treatment option with a manageable safety profile for a molecularly defined subset of glioblastoma patients. Its clinical benefit remains limited, underscoring the disease's heterogeneity and therapeutic resistance. The findings support the continued investigation of biomarker-guided ADC therapy and highlight the critical need for future clinical trials to integrate comprehensive molecular profiling for optimal patient selection.

Keywords: ABT-414; Depatuxizumab mafodotin; EGFR; glioblastoma; ocular toxicity.